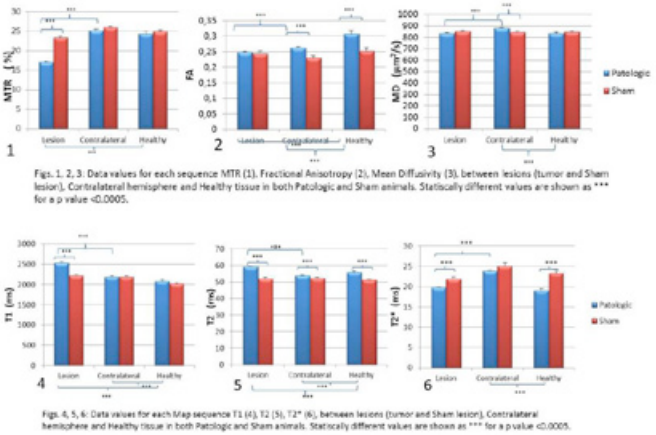
**Subjects and Methods:**
With the use of MRI relaxometry (before and after CA) of mouse brains with implanted tumors, we calculate quantitative maps (Q-maps) with an in house developed program. These Q-maps are used for the synthesization of different parametric weighted images offline and compared to standard acquired images of the same weightings.
**Results:** With the use of the SPARE technique, contrast between tissue increases and the noise, within the image, is reduced. It is further shown that unattainable parameters at the MR scanner can be achieving though synthesis, allowing for higher enhancement and tissue differentiation. Furthermore, SPARE using T2 Q-maps alone, allows visualization of CA enhance tumors and high image contrast between the bounding tissue.
**Discussion/Conclusion:** Parameter-weighted images reconstructed retrospectively with SPARE offers higher tissue contrast and reduced noise for different combination of TR and TE. Using the SPARE technique thus offers a solution for overcoming the lost contrast due to the convergence of T1 at high magnetic field strengths.
**References:**
1. Korb, J.P. and R.G. Bryant, Magn Reson Med, 2002. **48**(1): p. 21-6.
2. Rinck, P.A. and R.N. Muller, Eur Radiol, 1999. **9**(5): p. 998-1004.
3. Ortendahl, D.A., et al., Magn Reson Med, 1984. **1**(3): p. 316-38.
4. Zhu, X.P., C.E. et al., Br J Radiol, 1994. **67**(802): p. 976-82.

## 591

**Multimodal imaging in the characterization of a rat model of glioblastoma by using MRI and 18F-FDG PET/CT**

**M.C. Vieira-Leite**, P. López-Larrubia
*Experimental animals for human diseases, Instituto de Investigaciones Biomédicas Alberto Sols, madrid/SPAIN*

**Purpose/Introduction:** Glioblastoma is the most frequent primary brain tumour but despite the advances achieved in the last decades in treating human malignancies, its prognosis has not experienced a great change (1). In this line, magnetic resonance imaging (MRI) is the most used and versatile tool used nowadays (2), and PET/CT has become of clinical importance as it can also offer additional metabolic information with a high sensitivity (3,4). This study aimed to characterize a rat model of glioma C6, by using multiparametric MRI and comparing results with the data provided by 18F-FDG-PET/CT.
**Subjects and Methods:** Male Wistar rats (N=17) were submitted to a surgical injection of $10^5$ C6 cells in their right caudate-putamen. Sham animals (N=5) were used as a control group. All the individuals were studied with MRI, when tumour's volume was 10-100 $mm^3$, using a 7T system and the following protocol: T2, T2* and T1 weighted images to yield relaxation time maps, diffusion tension imaging (DTI) to obtain mean diffusivity (MD) and fractional anisotropy (FA) maps, and magnetization transfer (MT) to determine the MT ratio maps. Colour based maps were computed pixel-by-pixel, by fitting the signal to the appropriate equation, using a home-made software developed in Matlab. Data were analysed by selecting ROI's in the tumour, contralateral hemisphere and healthy tissue. Six animals (5 tumour-bearing and 1 control) were also submitted to an 18F-FDG-PET/CT study, analysing ROI's in the tumour, contralateral hemisphere and liver.
**Results:** Results are shown in figures 1-6. Tumour ROI´s compared with Sham animals, showed significantly different values of MTR, T1, T2 and T2*. The comparison between the tumour region and its contralateral hemisphere was also relevant on the MT, MD, T1, T2 and T2* measurements. By comparing the tumour and healthy tissue, there were significant differences on MT, FA, T1 and T2. PET/CT images showed tumour regions with significantly higher SUV values when compared to their contralateral, although a clear correlation between the SUV values and the MRI parameters could not be found.




Figs. 1, 2, 3: Data values for each sequence MTR (1), Fractional Anisotropy (2), Mean Diffusivity (3), between lesions (tumor and Sham lesion), Contralateral hemisphere and Healthy tissue in both Patologic and Sham animals. Statiscally different values are shown as *** for a p value <0.0005.




Figs. 4, 5, 6: Data values for each Map sequence T1 (4), T2 (5), T2* (6), between lesions (tumor and Sham lesion), Contralateral hemisphere and Healthy tissue in both Patologic and Sham animals. Statiscally different values are shown as *** for a p value <0.0005.

**Discussion/Conclusion:** There are significant differences in MRI parameters related to inflammation, oedema and hypoxia between tumour areas and both the contralateral hemisphere and healthy. 18F-FDG-PET/CT images provided a new type of information, which can be used additionally to the MRI data. This characterization can help in the proper selection and follow-up of patients who will benefit from tailored therapies, mainly those targeting angiogenesis and inflammation.
**References:**
1.Cancer.J, 2012;18:89–99
2.López-Larrubia,P. et al. Cap.12, ISBN:978-953-307-284-5
3.Am.J.Roent 2008;190:W365–W369
4.Am.J.Neuroradiol 2013;34:944-950

## 592

**Multiparametric MRI characterization of the tumoral and inflammatory microenvironmentof a glioma rat model in two growth stages.**

A. Amor-López, **P. López-Larrubia**
*Departamento de Modelos experimentales de enfermedades humanas, Instituto de Investigaciones Biomédicas, CSIC-UAM, Madrid/SPAIN*

**Purpose/Introduction:** Alterations in inflammation and microvasculature underlying the most complicated brain pathologies, like cancer. A deeper characterization of the inflammatory and tumoral microenvironment would improve the diagnosis and prognosis of neoplastic process and the validation of new-targeted therapies. In this line, MRI is established as a powerful tool for obtaining structural, functional and molecular information[1,2].
**Subjects and Methods:** Experiments were carried out using sham adult male Wistar (n=5) and glioma bearing animals in two stages of the tumor growth (early, n=10, tumors≤50μl; late, n=10 tumors≥75μl).
MRI experiments were performed on a 7.0-T horizontal system equipped with a $^1H$ selective birdcage resonator. The imaging protocol was: Magnetization transfer, MT (TR/TE= 2500/9.85 ms, 50 pulses, 5.5 μT, 1500 Hz); diffusion tensor imaging, DTI (TR/TE= 3000/40 ms, Δ/δ= 20/4 ms, 7 directions, b values 300 and 1400 s/$mm^2$); and dynamic contrast enhanced, DCE (TR/TE= 100/6 ms, 50 repetitions)
Images were computed on a pixel-by-pixel basis using My Map Analizer (in-house software developed in Matlab) and the obtained parametric maps were analyzed in three brain regions: tumor, contralateral hemisphere and apparently healthy tissue.
**Results:** Figures 1-4 depict the main results. Values measured in all cases showed significant differences between the regions and groups of animals assesed. Changes in MT and MD values are linked to the tumor progression,

the concomitant inflammation and edema. MT (fig.1) decreased in tumor compared with non-tumoral regions, and increases in late stages indicating alteration in the macromolecular-bound proton pool associated with the pathology and its progression. MD (fig.2) reflected the extension of the cellular swelling due to the inflammatory process, taking place in the brain just the tumor growing. Decreases in FA (fig.3) were correlated with the structural integrity loss in the brain because of the tumor´s presence. A higher ΔSI of larger tumors in DCE studies was in accordance with the expected increase in the disruption of the microvasculature in the late stages.

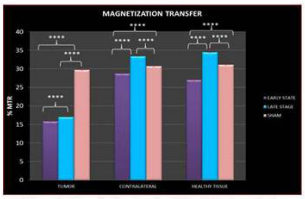



Figure 1. Magnetization transfer MRI obtained results by comparing rats with tumors in early and late stages, and Sham animals .(**** p ≤ 0.0001)

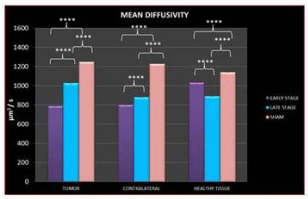



Figure 2. Mean diffusivity from diffusion tensor imaging obtained results by comparing rats with tumor in early and late stages, and Sham animals. (**** p ≤ 0.0001)

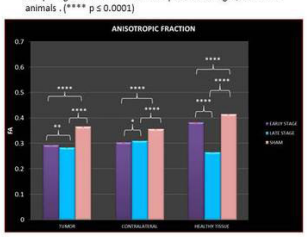



Figure 3. Anisotropic fractionfrom diffusion tensor imaging obtained results by comparing rats with tumor in early and late stages, and Sham animals. (**** p ≤ 0.0001)

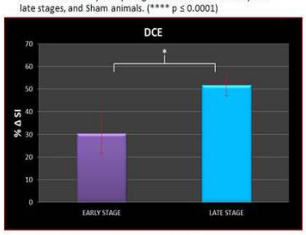



Figure 4. Changes in the signal intensity form DCE-MRI studies by comparing rats with tumors in early and late stages, and Sham animals (* p ≤ 0.05)

**Discussion/Conclusion:** Multiparametric MRI studies in this glioma model have allowed establishing clear and significant differences between regions in the brain, associated with the development not only of the tumor but also of the associated inflammation. MTR and MD measurements have clearly indicated that apparently healthy regions in the brain are actually affected in the late stage of the tumor development. DCE analysis indicate either an increased in the vascular permeability in large tumors compared with smaller ones.

**References:**

1.Lizarbe B. et.al, Neuroimage.2013, 64:448-457. 2. Lopez-Larrubia P. et.al, Cap.12, 2012, ISBN 978-953-307-284-5

## 593

### Molecular Imaging of Tumors and Metastases using Chemical Exchange Saturation Transfer (CEST) MRI

**M. Rivlin**[1], J. Horev[2], I. Tsarfaty[2], G. Navon[1]
*[1]School of Chemistry, Tel Aviv University, Tel Aviv/ISRAEL, [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv/ISRAEL*

**Purpose/Introduction:** The increased glycolytic rate and glucose avidity of malignant cells (Warburg effect) in comparison to normal tissue is the basis of the ability of FDG-PET imaging to accurately differentiate cancer from benign tissue regardless of morphology. The two glucose analogs 2-deoxy-D-glucose (2-DG) and 2-fluoro-2-deoxy-D-glucose (FDG) are preferentially taken up by cancer cells, undergo phosphorylation and accumulate in the cells. Both 2-DG and FDG have 4 hydroxyl residues, which are potential candidates for Chemical Exchange Saturation Transfer CEST NMR/MRI. The method enables to detect low concentrations of metabolites that contain residues with exchangeable protons such hydroxyl[1].
In the present work we take advantage of the enhanced accumulation of 2-DG and FDG in tumors to obtain large CEST values and would like to suggest either 2-DG-CEST or FDG-CEST as a potential replacement of PET/CT or PET/MRI in the clinic for the detection of tumors and metastases, distinguishing between malignant and benign tumors and monitoring tumor response to therapy.
**Subjects and Methods:** CEST-MRI experiments were performed on implanted xenograph mammary tumors ($DA_3$) of mice injected with 2-DG or FDG, scanned at 7T MRI. A series of gradient-echo images were collected from a single 1 mm axial slice after presaturation pulse, applied at several frequency offsets from the water, to produce the desired CEST effect[2].
**Results:** The tumor exhibited a CEST effect of about 20% for mice injected with 2gr/kg of 2-DG and about 30% for mice injected with 1gr/kg of FDG. These high values are the combined results originating from the injected glucose analogs, their phosphorylated products and from other metabolic products. The diagnostic benefit and uniqueness of this technique, is that the method is sensitive enough to detect regional differences in tumor uptake. We have shown that 2-DG CEST MRI enables to distinguish between the viable parts of tumor from the necrotic region of the tumor, unlike the conventional anatomical images.
**Discussion/Conclusion:** This novel imaging modality will also shed a new light on tumor basal metabolism, expression of tumor markers and the metabolic alteration induced by constitutive activation of oncogenes in tumor development. We expect that the developed novel imaging modality will enable early detection of tumors, tumor response to therapy, and tumors metabolism noninvasively by using MRI, without the need for radio-labeled isotopes.

**References:**

(1) Ward, K. M.; Aletras, A. H.; Balaban, R. S. **2000** *J Magn Reson*, *143*, 79.
(2) Zhou, J.; Zijl, P. C. M. v. **2006** *Progress in Nuclear Magnetic Resonance Spectroscopy*, *48*, 109.

## 594

### Robust Coregistration of Sestamibi SPECT and MR Images in Patients with High Grade Glioma: a revisited approach

J.-M. Tacchella[1, 2], E. Roullot[1], M.-E. Cohen[2], M. Lefort[2], M. Reynal[3], J.B. Martini[3], R. Guillevin[4], J.-Y. Delattre[5], G. Petrirena[5], M.-O. Habert[2, 6], N. Yeni[2, 6], A. Kas[2, 6], **F. Frouin**[2]
*[1]PRIAM, ESME SUDRIA, Ivry sur seine/FRANCE, [2]Laboratoire d'Imagerie Fonctionnelle, Inserm/UPMC, Paris/FRANCE, [3]Centre d'Acquisition et de Traitement des Images, UPMC, Paris/FRANCE, [4]Service de Radiologie, Université de Poitiers and CHU Poitiers, Poitiers/FRANCE, [5]Service de Neuro-oncologie, AP-HP, CHU Pitié-Salpêtrière, Paris/FRANCE, [6]Service de Médecine Nucléaire, AP-HP, CHU Pitié-Salpêtrière, Paris/FRANCE*

**Purpose/Introduction:** The usefulness of the Technetium-99m labeled Sestamibi SPECT modality in addition to the MRI modality has been suggested in therapy management for patients with high grade glioma [1]. The SPECT/MRI registration that is required for further data analysis is a complex preprocessing step due to the physiological distribution of the MIBI tracer. This work aims at proposing an efficient registration of SPECT/MRI data, which is optimized for each dataset.
**Subjects and Methods:** The database includes 62 SPECT/MRI datasets in patients with high grade glioma. The registration strategy consists in testing different methods and selecting the best one for each dataset thanks to a quantitative uptake criterion (UC), based on the physiological behavior of Sestamibi within particular anatomical structures [2]. The criterion relies on the high uptake of the tracer in the oculomotor muscles and pituitary gland and the low uptake in the eyeballs. Global strategy proceeds in 3 steps, embedded in the Brainvisa/Anatomist package: 1) a systematic application of 16 registration methods (Mn) derived from algorithms of Brainvisa and SPM software; 2) for each dataset, ranking of the 16 methods according to decreasing values of UC and selection of the best registration method, M* ; 3) visual assessment of M* as good, intermediate, or bad registration.